

Remarks

35 U.S.C. § 103

In the Office Action, the Examiner rejects claims 32, and 36-45 under 35 U.S.C. § 103(a) as being unpatentable over United States Patent No. 5,852,211 issued to Dumpelman et al. (hereinafter "Dumpelman") in view of EP Patent No. 0 174 624 issued to Bott et al. (hereinafter "Bott") (together "Cited References"). Applicants respectfully traverse the rejection.

In the Office Action, the Examiner indicates that the previously submitted arguments are unpersuasive since the claims do not exclude preparing the broth by a process including removing cells (biomass) such as by filtration. Applicants have amended the claims to clarify that the process for the recovery of an organic acid from a fermentation broth comprising the steps of conducting a fermentation to produce a fermentation broth, wherein the fermentation broth comprises an organic acid and microbial biomass and drying the fermentation broth to obtain an organic acid-containing dried product, wherein the drying occurs without prior removal of the microbial biomass from the organic acid-containing fermentation broth. Therefore, the claims now set forth how the initial fermentation was prepared prior to drying.

Applicants respectfully request reconsideration of the rejections based upon the Cited References with respect to the claims as currently amended. Certain basic considerations apply to obviousness rejections. The Manual of Patent Examining Procedures ("MPEP") describes the following tenets of patent law which must be adhered to:

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard with which obviousness is determined. *MPEP* §2141, citing *Hodosh v. Block Drug, Inc.*, 786 F.2d 1136, 1143 n.5, 229 U.S.P.Q 182, 187 n.5 (Fed. Cir. 1986).

Applicants respectfully submit that the Examiner has not presented a *prima facie* case of obviousness. For at least the reasons that all the limitations of the claims, as amended herein, are not in the Cited References, there is no motivation or suggestion in the prior art, and there was no reasonable expectation of success for the change in the processes of the Cited References.

All of the limitations of the claims must be present in the combination of references to reject the claims under 35 U.S.C. §103. Neither of the Cited References, however, disclose a process wherein drying occurs without prior removal of the microbial biomass from the organic acid-containing fermentation broth. Both Dumpelman and Bott describe a process comprising filtering to remove biomass prior to drying or crystallizing the desired product for separation from the broth. Therefore, an obviousness rejection is not complete. In addition, Dumpelman teaches away from simplifying the process by filtering prior to crystallization by stating that the object of the invention is to permit in the simplest possible manner the conversion of the sodium salt of 2-keto-L-gulonic acid, which is present in an aqueous, non-purified fermentation broth, into free 2-keto-L-gulonic acid in alcoholic solution in high yield and with high purity.

The Examiner has not indicated a motivation or suggestion in the prior art to modify the processes of Dumpelman or Bott that would result in the subject

matter of the claims of the subject application as required to form a *prima facie* case of obviousness..

A reasonable expectation of success is also required to have a *prima facie* case of obviousness. Applicants contend that one skilled in the art would not have a reasonable expectation of success of producing an organic acid by drying the fermentation broth without prior filtration of biomass. This is truly a surprising result. As evidence of this, Dumpelman with filtering of the fermentation broth prior to spray drying calls his process “simplest possible manner” of producing the organic acid. However, the method of the subject application is clearly more simple. The solid biomass and the crystallized byproduct acid are both removed in the same filtration step. Therefore, an obviousness rejection is not appropriate.

Example 1, as well as elsewhere in the specification as filed, provides a written description of the process as claimed. Example 1 of the subject application was performed wherein the drying occurs without prior removal of the microbial biomass from the organic acid-containing fermentation broth. The attached Declaration of Kevin Moore dated April 8, 2004 (“Declaration”) further describes the process performed in Example 1. The Declaration was previously filed in the United States Patent and Trademark Office with a response to an Office Action in the subject application’s parent application, United States Patent Application 10/09/631,638 filed on August 2, 2000 and is also relevant to this response to the Office Action. As stated in the Declaration, the fermentation of Example 1 was performed to produce a fermentation broth comprising both the organic acid and the biomass. The fermentation broth was subsequently spray dried without filtering to remove biomass, therefore the dried product contained substantially all the biomass produced in the fermentation.

United States Patent No. 5,834,231 (the “231 patent”) is referenced in Example 1. The ‘231 patent describes a process for the production of 2-keto-L-gulonic acid by the fermentation conversion of L-sorbose and/or sorbitol. The patent is referred to in Example 1 for the method of conducting the fermentation and not for the method of treating the whole fermentation broth. The Declaration clarifies the process used of Example 1. As stated, Example 1 of the Subject Application demonstrates the method of the claimed invention comprising conducting a fermentation to produce a fermentation broth, wherein the fermentation broth comprises an organic acid and microbial biomass, drying the fermentation broth to obtain an organic acid-containing dried product, wherein said drying occurs without prior removal of said microbial biomass from the organic acid-containing fermentation broth. The dried product may then be added to a lower alcohol in the presence of an acid, wherein said acid can be any acid which allows for selective recovery of the desired organic acid. A subsequent step is removing insolubles to obtain an organic acid, wherein the insolubles include the microbial biomass.

Specifically, Example 1 describes a process for the production of 2-keto-L-gulonic acid. The fermentation of Example 1 was prepared as described the ‘231 patent to produce a fermentation broth comprising an organic acid and microbial biomass. The fermentation was conducted in two steps as described in the ‘231 patent. As described in col. 5, lines 39-56, Strain ATCC 621 was used to convert sorbitol to sorbose. The fermentation included, as described in col. 6, additional components added to the medium including supplemental carbon sources (mannitol), nitrogen sources (Hysoy T and 10% corn steep liquor) and trace nutrients (Niacinamide, Thiamine, Pantothenic Acid, and Para amino benzoic acid). After conversion of sorbitol to sorbose the medium is pasteurization in an autoclave. The

sorbose was then converted to 2-keto-L-gulonic acid as indicated in column 6, lines 42-58. In the case of Example 1, the medium was inoculated with strain ADM 115-172, a mutant variant of NRRL B-21627. The conversion of sorbose to 2-keto-L-gulonic acid was aided by a "helper" strain of *B. Lichenformis* (ADM B102) as described in column 7, lines 15-38. Conversion of sorbose to 2-keto-L-gulonic acid is at a pH of 6.5, a temperature of 30°C with 1.5 vol./vol/min of air and a 275 rpm fermenter agitator speed for about 60 hours to prepare the fermentation broth comprising the organic acid and the microbial biomass. The fermentation broth comprised, as indicated in Example 1, 84 g/l 2-keto-L-gulonic acid, 4g/l sorbose and 136 g/l total dry solids including the microbial biomass ("whole fermentation broth").

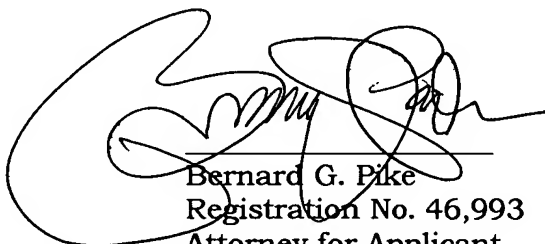
After the whole fermentation broth was prepared as described above, the whole fermentation broth was dried to obtain an organic acid-containing dried product, wherein the drying occurred without prior removal of the dry solids or the microbial biomass from the whole fermentation broth. The dried product was then further processed, as described in Example 1, by adding the dried product to a lower alcohol, anhydrous methanol, in the presence of an acid, sulfuric acid, finally removing the microbial biomass from the 2-keto-L-gulonic acid. The process as described was subsequently repeated and enables one skilled in the art to conduct the claimed invention.

As such, Applicants respectfully submit that the process as claimed is fully described, enabled, and not anticipated by the Cited References or any other references cited in the subject application. Reconsideration of the rejections is respectfully requested.

Conclusion

Applicants have made a diligent effort to fully respond to all the concerns and comments of the Examiner. Therefore, Applicants respectfully request that a timely Notice of Allowance be issued in the subject application. If the Examiner has any concerns regarding Applicants' present response, he is invited to contact Applicants' undersigned representative at the telephone number listed below so that those concerns may be expeditiously addressed.

Respectfully submitted,


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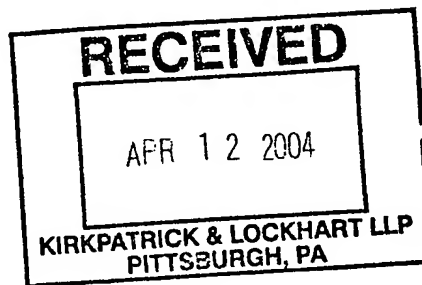
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : 09/631,638
First Named Inventor : Kevin M. Moore
Filing Date : August 2, 2000
TC/A.U. : 1651
Examiner : David M. Naff

Docket No. : 030592

Confirmation No.: 8662



Pittsburgh, Pennsylvania

Mail Stop: RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.132

I, Kevin Moore, hereby declare and state as follows:

1. I am a co-inventor of the invention as claimed in the above-referenced patent application (the "Subject Application").
2. I have reviewed Subject Application, including the claims and specification thereof, and understand the contents.
3. Example 1 of the Subject Application reads as follows:

A fermentation broth was prepared as described in U.S. Patent No. 5,834,231 containing 84 g/L 2-keto-l-gulonic acid, 4 g/L sorbose and 136 g/L total dry solids and spray dried on a high pressure nozzle sprayer (APV Americas; Tonawanda, New York). The feed was preheated to 170 °F, and dried with a 495 °F inlet and a 198 °F outlet temperature. A total of 8 gallons of feed was dried to give 10.2 lbs. of dried product as 8% moisture.

25 g of the spray dried product was slurried into 250 ml of anhydrous methanol. 3.2 ml of sulfuric acid was added to the solution over 20 minutes while stirring. The slurry was stirred for an additional 60 minutes, filtered and the solids washed with 150 ml of additional methanol. The product filtrate of 320 ml contained 35 g/L 2-keto-L-gulonic acid and 1.7 g/L of 2-keto-L-gulonic acid methyl ester. The cake of 12 grams contained 3.8% 2-keto-L-gulonic acid and 0.4% 2-keto-L-gulonic acid methyl ester, for a yield of 96%.

4. The fermentation of Example 1 was performed to produce a fermentation broth comprising both the organic acid and the biomass. The fermentation broth was subsequently spray dried without filtering to remove biomass, therefore the dried product contained substantially all the biomass produced in the fermentation. Example 1 provides an embodiment of the process as presently claimed.
5. U.S. Patent No. 5,834,231 (the "231 patent") describes a process for the production of 2-keto-L-gulonic acid by the fermentation conversion of L-sorbose and/or sorbitol. The patent further relates to novel bacterial strains useful in this process.
6. In the subject application, the Examiner has rejected the claims of the application as being unpatentable under 35 U.S.C. 103(a) as being unpatentable over Dumpelman (United States Patent No. 5,852,211) in view of Bott et al (European Patent No. 0 174 624).
7. As stated in the Declaration of Kevin Moore Under 37 C.F.R. §1.132 executed on August 18, 2003 (the "Previous Declaration"), I have read and understand Dumpelman et al. and an English translation of Bott et al. (the "Cited References") Neither of the Cited References disclose a process in which the fermentation broth is dried without first performing a filtration step. In addition, Dumpelman et al. teaches away from the filtering prior to crystallization by stating that the object of the invention is to permit in the simplest possible manner the conversion of the sodium salt of 2-keto-L-gulonic acid, which is present in an aqueous, non-purified

fermentation broth, into free 2-keto-L-gulonic acid in alcoholic solution in high yield and with high purity. For these reasons and the reasons set forth in the Previous Declaration, one skilled in the art would have no reasonable expectation of success of producing an organic acid by drying the fermentation broth without prior filtration of biomass.

8. Example 1 of the Subject Application demonstrates the method of the claimed invention comprising conducting a fermentation to produce a fermentation broth, wherein the fermentation broth comprises an organic acid and microbial biomass, drying the fermentation broth to obtain an organic acid-containing dried product, wherein said drying occurs without prior removal of said microbial biomass from the organic acid-containing fermentation broth. The dried product may then be added to a lower alcohol in the presence of an acid, wherein said acid can be any acid which allows for selective recovery of the desired organic acid. A subsequent step is removing insolubles to obtain an organic acid, wherein the insolubles include the microbial biomass.

Specifically, Example 1 describes a process for the production of 2-keto-L-gulonic acid. The fermentation of Example 1 was prepared as described the '231 patent to produce a fermentation broth comprising an organic acid and microbial biomass. The fermentation was conducted in two steps as described in the '231 patent. As described in col. 5, lines 39-56, Strain ATCC 621 was used to convert sorbitol to sorbose. The fermentation included, as described in col. 6, additional components added to the medium including supplemental carbon sources (mannitol), nitrogen sources (Hysoy T and 10% corn steep liquor) and trace nutrients (Niacinamide, Thiamine, Pantothenic Acid, and Para amino benzoic acid). After conversion of sorbitol to sorbose the medium is pasteurized. The sorbose was then

converted to 2-keto-L-gulonic acid as indicated in column 6, lines 42-58. In the case of Example 1, the medium was inoculated with strain ADM 115-172, a mutant variant of NRRL B-21627. The conversion of sorbose to 2-keto-L-gulonic acid was aided by a "helper" strain of *B. Lichenformis* (ADM B102) as described in column 7, lines 15-38. Conversion of sorbose to 2-keto-L-gulonic acid is at a pH of 6.5, a temperature of 30°C with 1.5 vol./vol/min of air and a 275 rpm fermenter agitator speed for about 60 hours to prepare the fermentation broth comprising the organic acid and the microbial biomass. The fermentation broth comprised, as indicated in Example 1, 84 g/l 2-keto-L-gulonic acid, 4g/l sorbose and 136 g/l total dry solids including the microbial biomass ("whole fermentation broth").

After the whole fermentation broth was prepared as described above, the whole fermentation broth was dried to obtain an organic acid-containing dried product, wherein the drying occurred without prior removal of the dry solids or the microbial biomass from the whole fermentation broth. The dried product was then further processed, as described in Example 1, by adding the dried product to a lower alcohol, anhydrous methanol, in the presence of an acid, sulfuric acid, finally removing the microbial biomass from the 2-keto-L-gulonic acid. The process as described was subsequently repeated and enables one skilled in the art to conduct the claimed invention.

9. I further declare that all statements made herein are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of

Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or document or any registration resulting therefrom.

Kevin M. Moore

Kevin M. Moore

April 8, 2004

Date



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
37 C.F.R. § 3.73(b) Statement

Applicants: Moore et al.

For: PROCESS FOR THE RECOVERY OF ORGANIC ACIDS

Serial No.: 10/041,635

Filed: January 10, 2002

Archer-Daniels-Midland Company (a Delaware corporation) is the assignee of the entire right, title and interest in the patent identified above by virtue of either:

- A. ☒ An assignment from the inventor(s) of the **patent application** identified above. The assignment was recorded in the United States Patent and Trademark Office on December 13, 2000 at Reel 011362, Frame 0471 or for which a copy thereof is attached.

OR

- B. ☐ A chain of title from the inventor(s) of the patent application identified above to the current assignee as shown below:

1. From ____ To: ____

The document was recorded in the United States Patent and Trademark Office on ____ at Reel __, Frame ____, or for which a copy thereof is attached.

☐ Copies of assignments or other documents in the chain of title are attached.

The undersigned (whose title is supplied below) is empowered to sign this statement on behalf of the assignee.

Power Of Attorney

I hereby revoke all previous powers of attorney, if any, and appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

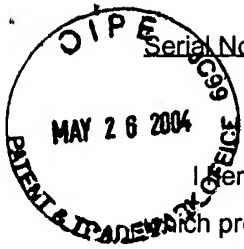
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Reg. No. 46,993
Reg. No. 43,027
Reg. No. 41,295
Reg. No. 54,771
Reg. No. 25,047
Reg. No. 46,150

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535 Smithfield Street
Pittsburgh, PA 15222-2312



Serial No. 10/041,635

PATENT

Declaration

I hereby declare that my presentation of this paper constitutes a certification under 37 C.F.R § 10.18, which provides, in part, that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application and any patent issuing therefrom.

Date

May 20, 2004

Signature

[Signature]

Name

David J. Smith

Title

Executive Vice-President, Secretary and General Counsel